Clinical Practice Recommendations for the Treatment of Alport Syndrome

A Synopsis for Families of Children with Alport Syndrome

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Alport syndrome is an inherited disorder of the kidneys that leads to kidney failure, especially in affected males. Boys with Alport syndrome have a 50% risk of needing dialysis or a kidney transplant by the age of 25 years. A group of nephrologists interested in Alport syndrome, the Alport Syndrome Research Collaborative (ARC), recently published recommendations for the treatment of Alport syndrome, with the goal of delaying the development of kidney failure in Alport patients.

What is the evidence that Alport syndrome can be treated?

Until recently most doctors thought that Alport syndrome was an untreatable disease. However, experiments carried out in mice with Alport syndrome showed that several different kinds of medication could slow down loss of kidney function. Preliminary studies in people with Alport syndrome have also provided support for the hypothesis that early treatment delays the onset of kidney failure.

What medications are recommended?

The recommended medications interfere with several hormones that together make up what is known as the renin-angiotensin-aldosterone system, or RAAS. The RAAS normally plays a very important role in maintaining the body’s fluid balance and blood pressure, helping to make sure that the kidneys get the blood flow necessary for good kidney function. The RAAS is overactive in various chronic kidney diseases and has been shown to promote scarring of the kidneys. Medications that interfere with RAAS hormones protect kidney function in animals and people with chronic kidney diseases.

Medications that interfere with RAAS hormones include:

1. angiotensin converting enzyme (ACE) inhibitors – these medications block the production of angiotensin II, the active form of angiotensin
2. angiotensin receptor blockers (ARBs) – these medications block the action of angiotensin II
3. aldosterone inhibitors – these medications block the action of aldosterone

Both ACE inhibitors and ARBs have been shown to slow down the loss of kidney function in mice with Alport syndrome. People with Alport syndrome who start
taking an ACE inhibitor while their kidney function is still normal are older when they develop kidney failure than Alport patients who don’t receive ACE inhibitors or are started on ACE inhibitors after they have started to lose kidney function. ACE inhibitors, ARBs and aldosterone inhibitors all reduce elevated urine protein levels in people with Alport syndrome.

We are still learning about the ways in which these medications protect the kidneys of animals and people with Alport syndrome. We believe there are at least two effects. First, these medications may directly prevent the formation of scar tissue in kidneys of animals and people with Alport syndrome. Second, by lowering urine protein levels these medications may prevent the harmful effects of high urine protein levels on kidney cells.

These medications have relatively few and minor side effects, they are not expensive and they have been used safely in many children with kidney disease. They are available all over the world and it is not necessary to travel to a special Alport syndrome center to receive treatment with these medications.

**When should the medications be started and how should they be used?**

We recommend regular measurement of urine protein levels in children with Alport syndrome, starting at 1 year of age and then at least annually. The test we use is called the urine protein-creatinine ratio. Children with urine protein-creatinine ratios above 0.2 should be treated with an ACE inhibitor with the goal of reducing the protein-creatinine as much as possible. This may require a gradual increase in the dose of the medication, and may be limited by side effects such as lightheadedness.

If a child is receiving the maximum dose of the ACE inhibitor and still has high urine protein levels, we recommend starting either an ARB or an aldosterone inhibitor (the choice is up to the child’s doctor).

**What are the possible side effects?**

Both ACE inhibitors and ARBs can cause lightheadedness, especially when a person stands up quickly. Sometimes these medications need to be stopped or their doses lowered because of persistent lightheadedness or fainting, but this is unusual. ACE inhibitors and ARBs should not be taken by females who are pregnant or who can become pregnant, because they can injure a developing fetus. ACE inhibitors, ARBs and aldosterone inhibitors can cause elevated blood potassium levels, but this is not a common problem in people who have normal kidney function.
A final word

Your child’s doctor is in the best position to help you determine if your child should be treated according to our recommendations. A detailed description of the recommendations written for nephrologists is available on the website of the Alport Syndrome Foundation (alportsyndrome.org).